A process for the preparation of acylphosphines

Description

5   The present invention relates to a process for the preparation of acylphosphines.

Mono- and bisacylphosphines are known in the state of the art as intermediates which are obtained when preparing mono- and bisacylphosphine oxide or mono- and bisacyl-phosphine sulfide compounds. These oxides and sulfides find diverse applications as

10   reactive initiators in the light-induced polymerisation of ethylenically unsaturated compounds.

US 4,298,738 discloses the preparation of monoacylphosphine oxides via reaction of diorganylphosphine chloride with an alcohol and subsequent reaction of the reaction

15   product with an acid halide. In EP-A 00 40721, monoacylphosphines are obtained from the reaction of acid halides with lithium diorganylphosphine, diorganylphos-phine or diorganyltrialkylsilylphosphine.

In Angew. Makromol. Chem. 199 (1992), 1-6, S. Banerjee et al. describe the prepara-

20   tion of poly(terephthaloylphosphine) via reaction of dilithium phenylphosphine with te-rephthaloyl chloride.

In Chem. Ber. 92 (1959), 3183-3189, Issleib et al., describe the preparation of acetyl diphenylphosphine via reaction of sodium diphenylphosphine with acetyl chloride.

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US 5,472,992, inter alia, carries out the preparation of bisacylphosphine oxide photo-initiators via reaction of the phosphine with the corresponding acid chloride in the pres-ence of a base with subsequent oxidation of the bisacylphosphine formed.
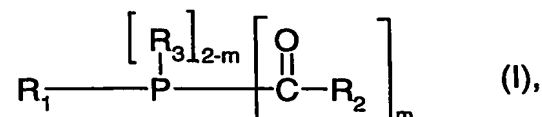
30   As the technology of the mono- and bisacylphosphine oxides is becoming increasingly important owing to the excellent photoinitiator properties of these compounds, there is also a need for highly practicable processes involving as little elaboration as possible for the preparation of the required intermediates, especially of the corresponding mono and bisacylphosphines, but also of the oxide and sulfide end products.

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WO 00/32612 describes a process by which it is possible to circumvent the use of the phosphine educts (R$_2$-PH, R-PH$_2$) which are undesirable because of their volatility, bad smell, toxicity and susceptibility to air and fire. The process is a one-pot process for the preparation of mono- and bisacylphosphines, where the starting material is a monoha-

40   logenophosphines or a P,P-dihalogenophosphine, which are less volatile, less toxic

and less susceptible to air. The organic phosphorous halides are reacted with an alkali metal in the presence of a catalyst to give a metallised phosphine, which is subsequently reacted with an acid halide to give the acyl phosphine.

5   It is an object of the present invention to improve the process described in WO 00/32612.

A process has been found for the preparation of acylphosphines of formula (I)

$$R_1\!-\!\!-\!\!-\!P\underbrace{\left[\begin{array}{c} R_3 \\ | \end{array}\right]_{2-m}}\left[\begin{array}{c} O \\ \| \\ C\!-\!R_2 \end{array}\right]_m \qquad (I),$$

10   wherein

m is 1 or 2;

15   R_1 is C_1-C_{18} alkyl, C_2-C_{18} alkyl which is interrupted by one or several non-successive O atoms; phenyl-substituted C_1-C_4 alkyl, C_2-C_8 alkenyl, phenyl, naphthyl, biphenyl, C_5-C_{12} cycloalkyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl, C_5-C_{12} cycloalkyl or the 5- or 6-membered O-, S- or N-containing heterocyclic ring
20   being unsubstituted or substituted by one to five halogen, C_1-C_8 alkyl, C_1-C_8 alkylthio and/or C_1-C_8 alkoxy;

  R_2 is C_1-C_{18} alkyl, C_3-C_{12} cycloalkyl, C_2-C_{18} alkenyl, phenyl, naphthyl, biphenyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals
25   phenyl, naphthyl, biphenyl or 5- or 6-membered O-, S- or N-containing heterocyclic ring being unsubstituted or substituted by one to four C_1-C_8 alkyl, C_1-C_8 alkoxy, C_1-C_8 alkylthio and/or halogen;

  R_3 is C_1-C_{18} alkyl, C_2-C_{18} alkyl which is interrupted by one or several non-
30   successive O atoms, phenylsubstituted C_1-C_4 alkyl, C_2-C_8 alkenyl, phenyl, naphthyl, biphenyl, C_5-C_{12} cycloalkyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl, C_5-C_{12} cycloalkyl or the 5- or 6-membered O-, S- or N-containing heterocyclic ring being unsubstituted or substituted by one to five halogen, C_1-C_{18} alkyl, C_1-
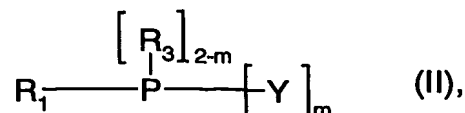35 C_8 alkylthio and/or C_1-C_8 alkoxy;

    by

(1)   reacting organic phosphorus halides of formula (II)

$$R_1 \overset{\displaystyle\left[\underset{R_3}{|}\right]_{2-m}}{—P—} \left[—Y \right]_m \qquad \text{(II)},$$
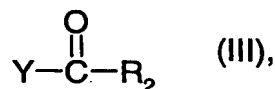
wherein R_1, R_3 and m have the meaning cited above;
and Y is Br or Cl,
with an alkali metal in a solvent in the presence of an activator, wherein the alkali metal is present in the form of a dispersion of alkali metal particles having a mean particle size of ≤ 500 μm in the solvent, and

(2)   subsequent reaction with m acid halides of formula (III)

$$Y—\overset{\displaystyle O}{\underset{\displaystyle ||}{C}}—R_2 \qquad \text{(III)},$$

wherein R_2 and Y have the meaning cited above,
which process is carried out without isolation of the intermediates.

C_1-C_{18} Alkyl is linear or branched and is, for example, C_1-C_{12}-, C_1-C_8-, C_1-C_6-, or C_1-C_4-alkyl. Examples are methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, pentyl, hexyl, heptyl, 2,4,4-trimethylpentyl, 2-ethylhexyl, octyl, nonyl, decyl, undecyl, dodecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl or octadecyl; C_1-C_{12}, C_1-C_8 and C_1-C_4 alkyl are also linear or branched and have, for example, the meanings cited above up to the corresponding number of carbon atoms.

C_2-C_{18} Alkyl, which is interrupted once or several times by non-successive -O-, is interrupted, for example, 1-9, e.g. 1-7, 1-5, 1-3 or 1 or 2 times by -O-, the O atoms always being interrupted by at least one methylene group. The alkyl groups may be linear or branched. The structural units obtained are thus, for example,
$-CH_2$-O-CH_3, $-CH_2CH_2$-O-CH_2CH_3, $-[CH_2CH_2O]_y$-CH_3, where y = 1-8,
$-(CH_2CH_2O)_7CH_2CH_3$, $-CH_2$-CH(CH_3)-O-CH_2-CH_2CH_3 or $-CH_2$-CH (CH_3)-O-CH_2-CH_3.

Phenyl-substituted C_1-C_4-alkyl is typically benzyl, phenylethyl, α-methylbenzyl, phenyl-butyl or α,α-dimethylbenzyl, preferably benzyl.

C_2-C_{18} Alkenyl radicals may be mono- or polyunsaturated, linear or branched and are, for example, allyl, methallyl, 1,1-dimethylallyl, propenyl, butenyl, pentadienyl, hexenyl or octenyl, preferably allyl. R_2 defined as C_2-C_{18} alkenyl is typically C_2-C_8, C_2-C_6, preferably C_2-C_4 alkenyl.

C_5-C_{12} Cycloalkyl is, for example, cyclopentyl, cyclohexyl, cyclooctyl, cyclododecyl, preferably cyclopentyl and cyclohexyl, more preferably cyclohexyl; C_3-C_{12} cycloalkyl is additionally e.g. cyclopropyl.

C_1-C_{18} Alkoxy is linear or branched radicals and is typically methoxy, ethoxy, propoxy, isopropoxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert-butyloxy, pentyloxy, hexyloxy, heptyloxy, 2,4,4-trimethylpentyloxy, 2-ethylhexyloxy or octyloxy, preferably methoxy, ethoxy, propoxy, isopropoxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert-butyoxy, most preferably methoxy.

Halogen is fluoro, chloro, bromo and iodo, preferably chloro and bromo, most preferably chloro.

Examples of O-, S- or N-containing 5- or 6-membered heterocyclic rings are furyl, thienyl, pyrrolyl, oxinyl, dioxinyl or pyridyl. The cited heterocyclic radicals may be substituted by one to five, e.g. by one or two, linear or branched C_1-C_8 alkyl, halogen and/or C_1-C_8 alkoxy. Examples of such compounds are dimethylpyridyl, dimethylpyrrolyl or methylfuryl.

Substituted phenyl, naphthyl or biphenyl is substituted by one to five, e.g. by one, two, three or four, preferably by one, two or three, for example linear or branched C_1-C_8 alkyl, linear or branched C_1-C_8 alkoxy or by halogen.

Preferred substituents for phenyl, naphthyl and biphenyl are C_1-C_4 alkyl, preferably methyl, C_1-C_4 alkoxy, more preferably methoxy, and chloro. Particularly preferred substituents are, for example, 2,4,6-trimethylphenyl, 2,6-dichlorophenyl, 2,6-dimethyl-phenyl or 2,6-dimethoxyphenyl.

R_2 is, for example, phenyl, preferably 2,4,6-trimethylphenyl, 2,6-dimethylphenyl or 2,6-dimethoxyphenyl, most preferably 2,4,6-trimethylphenyl.
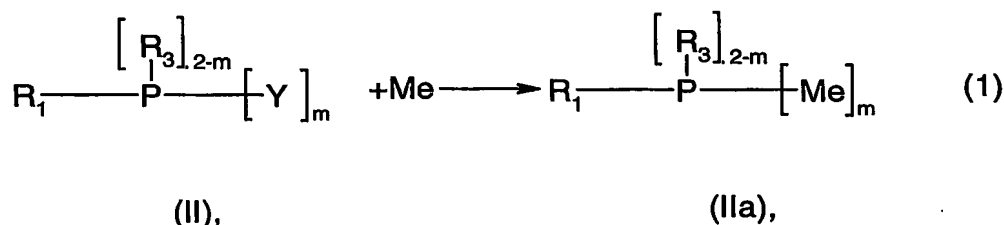
R_1 and R_3 are preferably unsubstituted phenyl or C_1-C_4 alkyl substituted phenyl, most preferably phenyl.

C_1-C_4 Alkoxyphenyl is phenyl which is substituted by one to four alkoxy radicals, for example 2,6-dimethoxyphenyl, 2,4-dimethoxyphenyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl or butoxyphenyl.

Within the scope of the present description and claims, "and/or" shall mean that not only one of the defined alternatives (substituents) may be present, but that also several different ones of the defined alternatives (substituents) may be present together, i.e. mixtures of different alternatives (substituents).

Within the scope of the present description and claims, "at least" shall be defined as "one" or "more than one", for example one or two or three, preferably one or two.

In the process of the invention for the preparation of mono- and bisacylphosphines, an organic phosphorus halide (II) is first reacted with an alkali metal, the metallised phosphine (IIa) being formed via different intermediary steps:

$$R_1 \overset{[R_3]_{2-m}}{\underset{\displaystyle P}{\rule{0pt}{0pt}}} [Y]_m \quad +Me \longrightarrow R_1 \overset{[R_3]_{2-m}}{\underset{\displaystyle P}{\rule{0pt}{0pt}}} [Me]_m \qquad (1)$$

(II),   (IIa),

R_1, R_3 and m have the meaning cited above, Me is an alkali metal.

Suitable alkali metals are, for example, lithium, sodium or potassium. It is also possible to use mixtures of these metals in the process of this invention. If lithium, sodium or potassium are used, then it is useful to employ from 4 to 8 atom equivalents of the alkali metal for the preparation of bisacylphosphines, and 2 to 4 atom equivalents of the alkali metal for the preparation of monoacylphosphines.

In a preferred embodiment of the process of the invention, sodium is used as the alkali metal.

The reaction (1) of the organic phosphorous halide with the alkali metal is carried out in a solvent. Suitable solvents are known aliphatic or aromatic solvents. Suitable solvents

are, for example, alcanes such as pentane, hexane, petroleum ether and ligroine, cycloalcanes such as cyclohexane and decalin, aromatic hydrocarbons such as toluene, ethyl benzene and tetralin, aliphatic, aromatic and mixed aliphatic-aromatic ethers, such as dimethyl ether, diethyl ether, methylpropyl ether, 1,2-dimethoxyethane, bis(2-
5   methoxyethyl) ether, dibutylether, methylphenylether and cyclic ethers, such as tetra-hydrofuran and dioxane. Toluol and ethyl benzene are preferably used. The reaction temperatures are preferably in the range from -20°C to +160°C, e.g. from 80°C to 120°C.

10   It is an essential feature of the process of the invention that the alkali metal Me is present in the reaction medium in the form of particles having a mean particle size of $\leq$ 500 µm, preferably $\leq$ 200 µm, more preferably $\leq$ 50 µm when reaction (1) is carried out. The lower limit for the mean particle size of the alkali metal particles is generally about 1 µm, preferably 5 µm, more preferably 10 µm. Alkali metal particles having the speci-
15   fied mean particle size can be readily produced by dispersing molten alkali metal in the reaction medium by means of a dispersing apparatus, preferably a turbine stirrer or a reaction mixing pump. A dispersion of alkali metal in the solvent is prepared in a suitable manner by adding alkali metal to a solvent, which is one or more of the solvents listed above, heating the mixture to a temperature above the melting point of the alkali metal, and vigorously stirring the mixture with a high speed turbine stirrer. The tem-
20   perature employed while dispersing the alkali metal in the solvent is in general $\geq$ 95 °C, for example from 95 °C to 200 °C for sodium, $\geq$ 64 °C, for example form 64 °C to 200 °C for potassium and $\geq$ 180 °C, for example from 180 °C to 250 °C for lithium. A stable dispersion is obtained, which can be cooled and kept below the melting point of the
25   alkali metal. In one embodiment of the inventive process, the alkali metal dispersion is prepared separately, cooled and subsequently transferred to a reaction vessel where it is reacted with the organic phosphorous halide to give the metallised phosphine (IIa).

The reaction (1) of the organic phosphorous halide with the alkali metal is carried out in
30   the presence of an activator. Suitable activators are aliphatic alcolols having 1 to 10 carbon atoms, preferably ethanol, 1-propanol, 2-propanol, n-butanol, iso-butanol, sec.-butanol and tert.-butanol, more preferably n-butanol, aromatic chlorohydrocarbons, preferably chlorobenzene, aliphatic chlorohydrocarbons, preferably 1-chloropentane, aromatic bromohydrocarbons, preferably bromobenzene, and aliphatic bromohydro-
35   carbons. Two or more different activators may be employed, which may be added at different stages of the reaction. Most preferred activators are n-butanol and chloroben-zene.
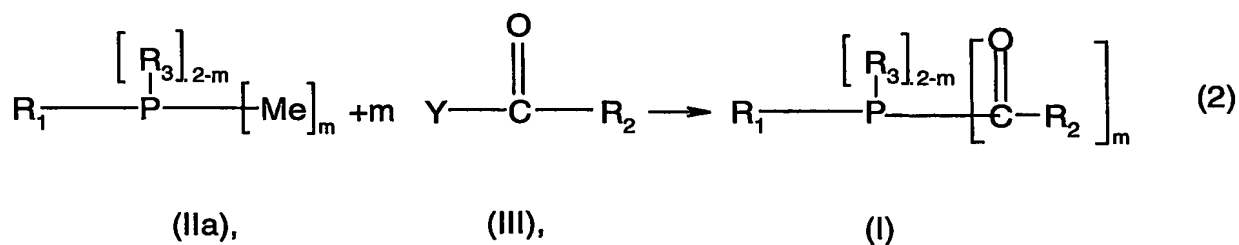
Each activator is present in the reaction mixture in an amount of 0,01 to 20 mol.-%
40   based on the amount of the alkali metal.

If chlorobenzene or 1-chloropentane is employed as an activator, it is added in an amount of in general from 0,1 to 20 mol-%, preferably from 1 to 10 mol-%, more preferably from 3 to 7 mol-%, based on the amount of the alkali metal. If an aliphatic alcohol is used as an activator, it is added in an amount of in general from 0,01 to 10 mol-%, preferably form 0,05 to 1 mol-%, based of the amount of the alkali metal.

Usefully, the organic phosphorous halide, optionally dissolved in a solvent which can be one or more of the solvents listed above, is added continuously to the alkali metal dispersion in the presence of the activator. Additional activator may be added at a later stage of the reaction. In a particularly preferred embodiment of the inventive process, sodium is employed as the alkali metal, and chlorobenzene and n-butanol are used as activators, in the amounts specified above. Chlorobenzene is present as a first activator in the alkali metal dispersion when the addition of the organic phosphorous halide starts. The organic phosphorous halide is added until the reaction stops to develop heat. At this point, n-butanol is added as a second activator, and the addition of organic phosphorous halide is continued. The reaction again starts to develop heat after the addition of the second activator, and the reaction continues to proceed. The n-butanol can be added all at once or in a continuous manner along with the organic phosphorous halide.

The metallised phosphine (IIa) obtained as described above is reacted in the next reaction step (2) with an acid halide (III) to the mono- or bisacylphosphine (I):

$$ R_1\!\!-\!\!\!-\!\!\!-\!\!P\overset{\left[\underset{|}{R_3}\right]_{2-m}}{-\!\!\!-}\!\!\left[Me\right]_m +m \;\; Y\!\!-\!\!\overset{\displaystyle O}{\overset{\|}{C}}\!\!-\!\!R_2 \;\longrightarrow\; R_1\!\!-\!\!\!-\!\!\!-\!\!P\overset{\left[\underset{|}{R_3}\right]_{2-m}}{-\!\!\!-}\!\!\left[\overset{\displaystyle O}{\overset{\|}{C}}\!\!-\!\!R_2\right]_m \qquad (2)$$

(IIa),   (III),   (I)

R_1, R_2, R_3, Me and m have the meaning cited above. Y is bromo or chloro, preferably chloro.

The solvents used may be, for example, the same as those used above for the first step. However, it is also possible to remove the solvent used in the first step by distillation and to take up the residue in another solvent and then to further process it.

It is preferred to work in the same solvent as in the preceding step, most preferably in toluene or ethylbenzene

5   The reaction temperatures for the reaction with the acid halide are usefully in the range from -20 to +120°C.

The mono- or bisacylphosphine of formula (I) can be isolated by the customary techno-logical methods which are known to the skilled person, for example by evaporation or distillation of the solvents and/or crystallisation. Likewise, the customary methods of
10   purification may be used, for example crystallisation, distillation or chromatography. Usefully, water is added to the reaction mixture in order to remove sodium chloride, the water phase is separated off and the product is isolated from the organic phase by dis-tilling off the solvents and/or by crystallisation of the product. The product can be fur-ther purified in the usual manner, for example by recrystallisation from a suitable sol-
15   vent.

However, the phosphines can also be reacted without isolation to the corresponding mono- or bisacylphosphine oxides or mono- or bisacylphosphine sulfides.

20   Depending an the substituents used, isomeric mixtures may be formed by the process of the invention.

Using the process of this invention it is also possible to prepare mono- and bisacyl-phosphines together in one reaction step.
25
By means of the process of the invention it is furthermore also possible to prepare mix-tures of aliphatic and aromatic monoacylphosphines or mixtures of aliphatic and aro-matic bis-acylphosphines. Mixtures of compounds of formula (II), wherein R_1 is an ali-phatic radical, and of compounds of formula (II), wherein R_1 is an aromatic radical, are
30   used in this case.

The acid halides (III) used as starting materials are known substances, some of which are commercially available, or may be prepared in analogy to known compounds.

35   From the acylphosphine of formula (I) obtained in reaction (2), acylphosphine oxides and acylphosphine sulfides of formula (IV)

$$R_1 - \overset{\overset{Z}{\|}}{\underset{[R_3]_{2\text{-}m}}{P}} - \left[\overset{\overset{O}{\|}}{\underset{3}{C}} - R_2 \right]_m \qquad \text{(IV)},$$
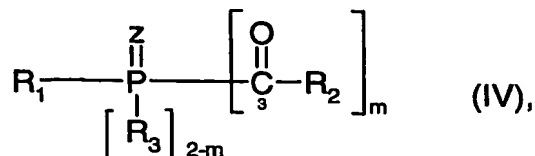
wherein

R_1, R_2, R_3 and m have the meaning cited in claim 1, and

5   Z is O or S,

can be prepared by oxidation or reaction with sulfur of the acylphosphine of formula (I).

The preparation of acylphospine oxides and acylphosphine sulfides from the acyl-

10   phosphines of the formula (I) is described in detail in WO00/32612.

The following Examples illustrate the invention in more detail.

Examples

15

Example 1: Preparation of bis–(2,4,6-trimethylbenzoyl)–phenylphosphine

(Activation by chlorobenzene and n-butanol, stirrer-type: turbine stirrer)

20   Under an inert atmosphere and with exclusion of moisture a dispersion of sodium (11.5 g; 0.50 mol) in toluene (100 ml) is produced by stirring with a high speed turbine stirrer with 11000 rpm at 105 °C resulting in sodium with a main particle size of less than 50 μm. The mixture is cooled to 30-35°C without stirring. Then the turbine stirrer is started again and chlorobenzene (2.8 g; 0.025 mol) is added dropwise and the contents of the

25   flask warms to 45-50°C. The resulting black suspension is heated to 100°C and P,P-dichlorophenylphosphine (19.7 g, 0.11 mol) is added dropwise at this temperature with exothermic behaviour. After the addition of ¼ of the whole amount of P,P-dichlorophenylphosphine the reaction stops to develop heat. At this point n-butanol (0.05 ml) is added and the exothermic reaction starts again. All the rest of the addition

30   of P,P-dichlorophenylphosphine stays exothermic. The resulting green suspension is stirred at 100-110°C for 30 min. The mixture is cooled to 75°C and 2,4,6-trimethylbenzoylchloride (43.8g; 0.24 mol) is added dropwise over a period of 30 min at this temperature. An exothermic reaction was observable. To the brown suspension was added toluene (200 ml) and the mixture was stirred for 60 min at 70-85°C. The

35   mixture was hydrolysed with water (150 ml) and the phases were separated. The prod-

uct phase was analysed by ^{31}P-NMR. This showed the desired bis—(2,4,6-trimethylbenzoyl)—phenylphosphine with 85-90% purity.

Comparative example 1: Preparation of bis—(2,4,6-trimethylbenzoyl)—phenylphosphine

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(Activation by chlorobenzene and n-butanol, stirrer-type: standard blade stirrer)

Under an inert atmosphere and with exclusion of moisture a dispersion of sodium (11.2 g, 0.50 mol) in toluene (200 ml) is produced by stirring with a standard blade stirrer with
10   1500 rpm at 105 °C resulting in sodium with a main particle size of 950 μm. The mixture is cooled to 30-35°C without stirring. Then the stirrer is started again with 300 rpm and chlorobenzene (2.93 g, 0.026 mol) is added dropwise without any visible effects. Then n-butanol (0.1 ml) is added and the mixture is heated to 40-50°C leading to a black coloured suspension. This suspension is heated to 100°C and P,P-
15   dichlorophenylphosphine (20.4 g, 0.114 mol) is added dropwise at this temperature with exothermic behaviour. After the addition of ¼ of the whole amount of P,P-dichlorophenylphosphine the reaction stops to develop heat. At this point n-butanol (0.05 ml) is added and the exothermic reaction does not start again. The addition of n-butanol (0.05 ml) is repeated and the exothermic reaction starts again. All the rest of
20   the addition of P,P-dichlorophenylphosphine stays exothermic. The resulting brown suspension is stirred at 95-105°C for 60 min. The mixture is cooled to 75°C and 2,4,6-trimethylbenzoylchloride (45.85 g, 0.251 mol) is added dropwise over a period of 30 min at this temperature. An exothermic reaction was observable only for the first 10% of the total amount of 2,4,6-trimethylbenzoylchloride. The suspension is stirred at 90°C
25   for 90 min. The mixture was hydrolysed with water (200 ml) and the phases were separated. The product phase was analysed by ^{31}P-NMR. This showed the desired bis—(2,4,6-trimethylbenzoyl)—phenylphosphine only in traces (ca. 1%).

30   Example 2: Preparation of bis—(2,4,6-trimethylbenzoyl)—phenylphosphine oxide

(Activation only by n-butanol, stirrer-type: turbine stirrer)

Under an inert atmosphere and with exclusion of moisture a dispersion of sodium (11.5
35   g, 0.50 mol) in toluene (100 ml) is produced by stirring with a high speed turbine stirrer at 105 °C. With further stirring at 100°C, n-butanol (0.05 ml) is added. To the resulting grey suspension is added P,P-dichlorophenylphosphine (21.5 g, 0.12 mol) dropwise over a period of 20 min with constant development of exothermic heat. The mixture is then stirred. for 30 min at 100-110°C and toluene (100 ml) was added. Then 2,4,6-
40   trimethylbenzoylchloride (49.3 g, 0.,27 mol) was added dropwise over a period of 30

min at 70-80°C. Only during the first 20% of the addition of 2,4,6-trimethylbenzoylchloride an exothermic reaction is observable. The reaction temperature is increased to 85°C and later to 110°C so to allow the exothermic reaction. The mixture is stirred at 110°C for 30 min. The temperature is lowered to 40°C and H_2O_2

5   (30%, 17.0 g, 0.15 mol) and water (150 ml) are added dropwise. The reaction is stirred at a temperature between 40 and 60°C for 2 h. The phases were separated. The product phase was analysed by ^{31}P-NMR. This showed the desired bis–(2,4,6-trimethylbenzoyl)–phenylphosphine oxide with 25% purity.